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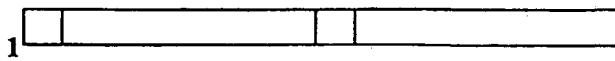
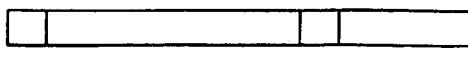
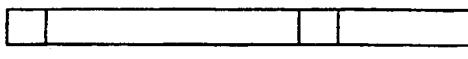
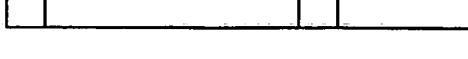
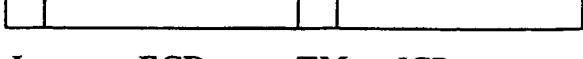
(10) International Publication Number
WO 03/087380 A1(51) International Patent Classification⁷: **C12N 15/54, 15/09, 15/11, 15/63, 9/10, C07K 16/40, C12N 5/10, A61K 31/711, 31/713, 38/45, 39/395**(74) Agent: **EINAV, Henry; INTER-LAB LTD. SCIENCE BASED INDUSTRIAL PARK, KIRYAT WEIZMAN, 76110 NESS ZIONA (IL).**(21) International Application Number: **PCT/IL03/00317**(81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.**(22) International Filing Date: **15 April 2003 (15.04.2003)**(84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).**(25) Filing Language: **English**(26) Publication Language: **English****Published:**

- with international search report
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(57) Abstract: This invention relates to the use of NIK and related molecules for the modulation of signal activities controlled by cytokines, and some new such molecules.

INTERNATIONAL SEARCH REPORT

10151314

Rec'd PCT/PTO 1 OCT 2004

Int'l Application No
PCT/IL 03/00317

A. CLASSIFICATION OF SUBJECT MATTER

| | | | | | |
|-------|------------|-----------|------------|------------|-----------|
| IPC 7 | C12N15/54 | C12N15/09 | C12N15/11 | C12N15/63 | C12N9/10 |
| | C07K16/40 | C12N5/10 | A61K31/711 | A61K31/713 | A61K38/45 |
| | A61K39/395 | | | | |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|---------------------------|
| X | <p>DATABASE GENESEQ 'Online! EBI, Hinxton, Cambridgeshire, U.K.; 4 March 1999 (1999-03-04)</p> <p>ROTHE M, & WU L,: "Human NIK protein." Database accession no. AAW82497 XP002249620 abstract & US 5 854 003 A (ROTHE MIKE ET AL) 29 December 1998 (1998-12-29) column 13 -column 20; claim 6</p> <p>----</p> <p style="text-align: center;">-/-</p> | 42-49, 51,52, 54,55 |

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

30 July 2003

Date of mailing of the international search report

12/08/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Intern'l Application No
PCT/IL 03/00317

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|--|
| X | <p>DATABASE GENESEQ 'Online! EBI, Hinxton, Cambridgeshire, U.K.; 15 April 1998 (1998-04-15)</p> <p>BOLDIN M ET AL.: "Amino acid sequence of NF-kappaB inducing kinase." Database accession no. AAW42402 XP002249621 abstract & WO 97 37016 A (BOLDIN MARK; METT IGOR; WALLACH DAVID; MALININ NIKOLAI) 9 October 1997 (1997-10-09) figure 6</p> <p>---</p> | 42-49, 51,52, 54,55 |
| X | <p>MALININ NIKOLAI L ET AL: "MAP3K-related kinase involved in NF-kappa-B induction by TNF, CD95 and IL-1." NATURE (LONDON), vol. 385, no. 6616, 1997, pages 540-544, XP002036441 ISSN: 0028-0836 page 540 -page 544</p> <p>---</p> | 42-49 |
| A | <p>EP 0 578 932 A (AJINOMOTO KK ;SUGAMURA KAZUO (JP)) 19 January 1994 (1994-01-19)</p> <p>the whole document</p> <p>-----</p> | 1-6, 8-18, 20-28, 30-32, 34-39, 41-49, 51,52, 54-70, 72-74 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL 03/00317

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-8, as far as in vivo methods are concerned, and claims 20-29, 66-74 are directed to a method of treatment of the human or animal body, the search has been carried out and based on the alleged effects of the compound or composition.
2. Claims Nos.: 7, 19, 29, 33, 40, 50, 53, 56 (partially), 71 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Claims Nos.: 7, 19, 29, 33, 40, 50, 53, 56 (partially), 71

Claims 7, 19, 29, 33, 40, 50, 53, 56 (partially), 71 refer to "small molecules" without giving a true technical characterisation of said "small molecules." Moreover, no such "small molecules" are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Articles 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.